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10/565,718	08/28/2006	Yongli Yu	CSPTAL31.001APC	6129

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EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
04/17/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/565,718	YU ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/28/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is responsive to communication filed 8/28/2006. The status of the claims is as follows: claims 1-10 and 17-22 are under current examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Enablement is considered in view of the *Wands* factors.

Nature of the invention. The claims are drawn to a method of preventing or treating various diseases caused by a virus comprising treatment with a CpG-containing ODN.

Scope of the claims. The claims are broad in that they encompass all diseases, including those that are caused by single-stranded positive strand RNA viruses (see claims 18-19) as well as the coronavirus and flaviviridae virus families (see claim 20). Further, the claims are drawn to widely different viruses, including SARS, HCV, dengue virus and the Japanese encephalitis virus (see claims 21-22).

State of the prior art. The prior art discloses the use of CpG ODNs containing compositions (see art rejection below). Further, CpG ODNs are widely known to induce

immune responses. Additionally, the instant specification provides the following recitation in paragraph 2 (DESCRIPTION OF THE RELATED ART): “Recently, studies have demonstrated that many bacterial and viral DNAs possessing CpG structure represent a danger signal for human immune system and are capable of activating a variety of immune cells to initiate the defense mechanism of body against the bacteria and virus. CpG is a dinucleotide formed by the connection of cytosine and guanine through phosphoric acid, wherein C denotes cytosine, G denotes guanine and p denotes phosphoric acid. Further studies indicate that artificial single-stranded oligodeoxynucleotide DNA containing one or more CpG(s) (CpG ODN) can also show potent immunoenhancing and immunoregulatory function, activate a variety of immune cells to start the defense mechanism of body against virus, and exhibit a promising potential for clinic application.”

Guidance in the specification. There is none. More specifically, the specification provides a discussion of relevant art, methods of making such ODNs and their effects on different diseases *in vitro*. No real data is demonstrated. Of note, the single figure provides no useful information. Figure 1 merely shows a culture well plate with liquid in it.

Working examples. The working examples provide disclosures related to the method steps of making the ODNs and their effects on different viruses on PBMCs. No in vivo data or data showing the successful treatment or prevention of viral disease is demonstrated. Of note, the examples fail to characterized what the "antiviral" substances are.

Predictability of the art. There is no way the ordinary artisan can predict a successful treatment for the broadly claimed viruses as well as those specifically claimed.

Undue experimentation. Much undue experimentation is necessary for the claimed method if even possible at all. Such a treatment would require data at many more biological levels, including cellular, physiological and whole organism. The specification is not clear in identifying what the "antiviral" substances are that is being specifically released by the PBMCs and thus, the specification fails to disclose the underlying mechanisms of the “treatments”. Further, it is not clear that viral inhibition can be achieved at the level of the whole organism.

Because of the discussion above, there would be much undue experimentation for the ordinary artisan to practice the claimed method.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 9 and 17-21 are rejected under 35 U.S.C. 102(a) as being anticipated by CN031408214 (cited, hereinafter as “Bao”).

The cited reference discloses a series of artificial CpG-containing single-stranded ODNs, each of which contains one or more CpGs, wherein the ODNs can stimulate PBMCs to produce antiviral substances in protecting against the SARS virus (see Abstract). More specifically, the sequences set forth as SEQ ID NOs: 1-5 (see claim 2) by the instant application are disclosed by Bao on page 3 as DVAX-1, 3, 4, 5 and 6.

Claims 1, 3-5, 7-10, 17-20 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 6218371 (cited, hereinafter as "Krieg") as evidenced by Sheehan et al (2003).

Krieg disclosed both methods and products for stimulating the immune system using immunotherapeutic oligonucleotides and cytokines (see whole document). More specifically, the invention is drawn to synergistic combinations of CpG oligos and cytokines and their use in stimulating immune response (see Abstract). The authors provide the following recitation with respect to synergism: "The combination of immunopotentiating cytokine and CpG oligonucleotide showed induction of Th1 specific antibody when immunopotentiating cytokine alone only produced Th2 specific antibody" (see paragraph 98). See Figures 1-9 demonstrating the potentiation of the immune response following CpG oligo treatment, including antibody production and modulation of MHC Class I and II responses. Further, the authors identify a number of diseases in which the invention is useful for treatment; they include influenza virus (see paragraph 20), hepatitis C virus (paragraph 20), Dengue virus (paragraph 34), and Japanese encephalitis virus (paragraph 34). Paragraph 34 also discloses coronavirus while the Flaviviridae family is

disclosed in paragraph 43. With respect to the limitations in claims 8, the authors make the following recitation in paragraph 107: "For use in vivo, nucleic acids are preferably relatively resistant to degradation (e.g. via endo- and exo-nucleases). Secondary structures, such as stem loops, can stabilize nucleic acids against degradation. Alternatively, nucleic acid stabilization can be accomplished via phosphate backbone modifications as discussed above. A preferred stabilized nucleic acid can be accomplished via phosphate backbone modifications. A preferred stabilized nucleic acid has at least a partial phosphorothioate modified backbone. Phosphorothioates may be synthesized using automated techniques employing either phosphoramidate or H-phosphonate chemistries. Aryl- and alkyl-phosphonates can be made for example as described in U.S. Pat. No. 4,469,863; and alkylphosphotriesters (in which the charged oxygen moiety is alkylated as described in U.S. Pat. No. 5,023,243 and European Patent No. 092,574) can be prepared by automated solid phase synthesis using commercially available reagents. Methods for making other DNA backbone modifications and substitutions have been described (Uhlmann, E. and Peyman, A., 1990, Chem. Rev. 90:544; Goodchild, J., 1990, Bioconjugate Chem. 1:165). 2'-O-methyl nucleic acids with CpG motifs also cause immune activation, as do ethoxy-modified CpG nucleic acids. In fact, no backbone modifications have been

found that completely abolish the CpG effect, although it is greatly reduced by replacing the C with a 5-methyl C." Sheehan et al (2003) provides discussion related to the structure of phosphorothioate sulfur (see page 4116).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 5 of copending Application No. 11/720070. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a single stranded CpG-containing sequence wherein the bases may be sulfur-modified.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michelle Horning/
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648